HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2016 July 01.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2015 July 1; 69(3): e93–e99. doi:10.1097/QAI.0000000000000644.

Maternal Combination Antiretroviral Therapy is Associated with Improved Retention of HIV-Exposed Infants in Kinshasa, Democratic Republic of Congo

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Abstract

Background—Programs to prevent mother-to-child HIV transmission (PMTCT) are plagued by loss to follow-up (LTFU) of HIV-exposed infants. We assessed if providing combination antiretroviral therapy (cART) to HIV-infected mothers was associated with reduced LTFU of their HIV-exposed infants in Kinshasa, DR Congo.

Methods—We constructed a cohort of mother-infant pairs using routinely collected clinical data. Maternal cART eligibility was based on national guidelines in effect at the time. Infants were considered LTFU following three failed tracking attempts after a missed visit or if more than six months passed since they were last seen in clinic. Statistical methods accounted for competing risks (e.g. death).

Results—1318 infants enrolled at a median age of 2.6 weeks (interquartile range [IQR]: 2.1-6.9), at which point 24% of mothers were receiving cART. Overall, 5% of infants never returned to care following enrollment and 18% were LTFU by 18 months. The 18-month cumulative incidence of LTFU was 8% among infants whose mothers initiated cART by infant enrollment and 20% among infants whose mothers were not yet on cART. Adjusted for baseline factors,

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Meetings at which parts of the data were presented as a poster: 47th Annual Society for Epidemiologic Research Meeting, Seattle, WA June 24-27, 2014.

AUTHOR CONTRIBUTIONS

L.F. conceptualized and designed the study and conducted analyses under the guidance of all coauthors. L.F., A.E., V.O., J.L.C., P.N., J.L., A.V.R., and F.B. were collaborators on the parent project (the UNC-DRC program) that supplied data for this secondary analysis and oversaw data collection and quality. V.O., J.L.C., P.N., and J.L. directed implementation of clinical protocols. L.F. drafted the initial manuscript and revisions were made by all coauthors. All coauthors approved the final draft. We are grateful for the patient care, program administration and coordination, and data entry contributions provided by the entire UNC-DRC program staff.

CONFLICTS OF INTEREST

There are no conflicts of interest.

infants whose mothers were not on cART were over twice as likely to be LTFU, with a subdistribution hazard ratio of 2.75 (95% confidence limit: 1.81, 4.16). The association remained strong regardless of maternal CD4 count at infant enrollment.

Conclusion—Increasing access to cART for pregnant women could improve retention of HIV-exposed infants, thereby increasing the clinical and population-level impacts of PMTCT interventions and access to early cART for HIV-infected infants.

Keywords

HIV-exposed infants; Prevention of mother-to-child HIV transmission (PMTCT); Pediatric HIV; Loss to follow-up; Retention in care; Democratic Republic of Congo

INTRODUCTION

Despite the scale-up of prevention of mother-to-child HIV transmission (PMTCT) programs worldwide, an estimated 260,000 children continue to be infected with HIV each year. [1] The ongoing pediatric HIV epidemic and associated mortality is driven in part by the overwhelming number of HIV-exposed infants who are lost to follow-up (LTFU) from PMTCT care. A recent meta-analysis of 11 studies conducted in sub-Saharan Africa estimated that 34% of HIV-exposed infants are lost from care by three months of age, with some settings reporting over 70% LTFU. [2] Available antiretroviral regimens can greatly reduce vertical HIV transmission, [3] but only a marginal impact on population-level transmission will be achieved if program retention remains low. [4]

At the clinical level, ensuring HIV-exposed infants are retained in care is necessary to administer HIV tests, provide prophylactic regimens, monitor breastfeeding, and provide other services such as vaccinations. LTFU of HIV-exposed infants also impedes early initiation of combination antiretroviral therapy (cART) for HIV-infected infants. Early cART initiation is critical because, without treatment, a third of infants will die within the first year of life and half within two years. [5,6]

Despite the importance of retaining HIV-exposed infants in care, few modifiable risk factors for infant LTFU are known. Evidence suggests that HIV-infected adults who receive cART are less likely to be LTFU than those who do not receive cART. [7] As HIV-exposed infants depend on their caregivers to bring them to care, we hypothesized that provision of cART to HIV-infected caregivers may also play a role in the retention of their infants. The goal of this study was to assess if providing cART to HIV-infected mothers was associated with reduced LTFU of HIV-exposed infants in a large HIV program in Kinshasa, Democratic Republic of Congo (DRC) where the prevalence of HIV among women seeking antenatal care is estimated to be 2%. [8]

METHODS

Study population

We used data from HIV-exposed infants who received care between January 1, 2007 and July 31, 2013 in a family-centered HIV program implemented at two centralized sites in

Kinshasa with technical assistance provided by the University of North Carolina at Chapel Hill (UNC-DRC program). The study clinics, which were integrated into the existing healthcare system in Kinshasa and supervised by the government, provided comprehensive care (including routine PMTCT services) to individuals identified through a large referral network that included 90 antenatal care facilities and 32 TB clinics. Enrollees were classified as 'exposed infants' if they were <18 months of age at the time of enrollment and did not yet have a confirmed HIV-positive diagnosis. HIV exposure was confirmed by a positive HIV antibody test in the mother or in the infant at <18 months of age.

We linked routinely collected data from HIV-exposed infants with data from their mothers to construct a cohort of mother-infant pairs. So that all infants could experience the entire 18-month follow-up period, we only included infants who were enrolled before January 1, 2012. Infants enrolled after 18 months of age and those who could not be matched to a mother receiving care in the UNC-DRC program by the time of infant enrollment were excluded. Since duration of maternal enrollment in care may be an important confounder and modifier of the relationship between maternal cART status and infant LTFU, we additionally excluded infants whose mothers enrolled in the UNC-DRC program before their most recent pregnancy.

Clinic visits for HIV-exposed infants were scheduled to occur every four weeks from the first visit at two weeks of age through 18 weeks of age and then every three months thereafter, with additional visits scheduled as clinically needed. Infants were considered confirmed HIV-negative and deactivated from care if they received a negative HIV virologic or serologic test result obtained more than three months after the cessation of breastfeeding. HIV-exposed infants diagnosed with HIV were eligible to receive ongoing HIV care and treatment in the UNC-DRC program. [9,10] For infants <18 months of age, HIV was diagnosed by virologic testing, with initial testing at six weeks of age and confirmatory virologic testing of all positive results performed on a second specimen. DNA PCR assays were implemented in Kinshasa in November 2009. Before that time, HIV RNA assays were the only available virologic HIV test and stock outs were frequent. Additional details on the program background and services provided to HIV-exposed infants are published elsewhere. [11]

Definitions and Statistical analysis

Baseline was defined as infant enrollment and the outcome of interest was LTFU before confirmation of an HIV-positive or -negative status. Infants were considered LTFU on their last attended clinic visit date following three failed tracking attempts after a missed appointment or if more than six months passed since they were last seen in the clinic. The six-month cutoff was chosen based on empirical evidence from adult HIV treatment programs, which suggests that a cutoff of six months from the last attended clinic visit results in the least amount of outcome misclassification. [12] Infants who never returned for a follow-up visit were assigned a survival time of one day.

The primary exposure was baseline maternal cART status. The reference group included infants whose mothers initiated cART by the day of infant enrollment, which was provided according to World Health Organization (WHO) guidelines in effect at the time. Before

2010, all women with a CD4 cell count <200 cells/mm^3 were eligible for cART [13]. In 2010, the immunological cutoff increased to 350 cells/mm^3 [14].

Baseline characteristics of infants and their mothers were summarized using standard descriptive statistics. Infants were considered underweight if they had a weight-for-age Z-score (WAZ) and stunted if they had a height-for-age Z-score (HAZ) more than two standard deviations below the median value for a given age group and sex. Z-scores were derived from the WHO Child Growth Standards [15] using the WHO Anthro software (version 3.2.2, January 2011) and SAS macro. Growth status was based on the first available weight or height values measured within a month of enrollment. Maternal CD4 counts were based on the first available measurement within three months of infant enrollment.

All analyses were conducted in SAS 9.3 (SAS Institute, Inc., Cary, North Carolina). Accounting for competing risks, [16] the 18-month cumulative incidence of infant LTFU was estimated within strata of maternal cART status and baseline covariates. To quantify the association between maternal cART and infant LTFU, we used the SAS macro %PSHREG [17] to implement the proportional subdistribution hazards model of Fine and Gray [16,18]. Crude and covariate-adjusted hazard ratios (HR), as well as corresponding 95% confidence limits (CL), were generated. In these analyses, follow-up began at infant enrollment and continued until the first of the following: the event of interest (LTFU), a competing event (death or graduation from care), or a censoring event (18 months of age or August 2013). Graduation from care was defined as being deactivated from care after confirmation of an HIV-negative status or transfer to ongoing HIV care and treatment following confirmation of an HIV-positive status. We also provide cause-specific HRs estimated from a Cox model for comparison.

Covariates included the baseline variables infant age, infant WAZ, maternal age, maternal CD4 count, maternal enrollment duration (defined as days since maternal enrollment in the UNC-DRC program), and time since the beginning of the study (defined as days between January 1, 2007 and the date of infant enrollment). The covariates were modeled with Stone and Koo's additive splines constrained to be linear in the tails, with knots at the 5th, 35th, 65th, and 95th percentiles [19]. To avoid excluding individuals with missing covariate data from the analysis, missing values were imputed using the sequential regression method described by Raghunathan et al. [20] and implemented in IVEware 0.2 (Institute for Social Research, University of Michigan, Ann Arbor, Michigan). Five complete datasets were generated and analyzed separately using standard statistical procedures. Results from the five complete datasets were combined using MIANALYZE procedures in SAS, which produce variance estimates that properly reflect the uncertainty due to missing values. To assess whether our results were sensitive to imputation assumptions, in a sensitivity analysis we compared results from the imputation analysis to results from a model that excluded the 122 individuals with any missing covariate data (i.e. a complete-case analysis). While complete-case analysis is the most frequently implemented method for handling missing data and the default method in most commonly used statistical software programs, precision is reduced due to the diminished sample size and results from such analyses may be biased if the data are not missing completely at random. [21]

Secondary analysis

To inform the question of whether providing HIV-infected mothers with cART reduces LTFU of their HIV-exposed infants regardless of the health status of the mother, we secondarily assessed the HR for the effect of maternal cART on infant LTFU stratified by maternal CD4 cell count (<350 or 350+) at infant enrollment.

Ethics statement

All research was approved by the Ethics Committee of the Kinshasa School of Public Health and the University of North Carolina at Chapel Hill Institutional Review Board.

RESULTS

1736 HIV-exposed infants enrolled into care during the study period, of which 1318 were included in the analysis after exclusion criteria were applied (Figure 1). Infants included in the analysis enrolled at a median age of 2.6 weeks (interquartile range [IQR]: 2.1-6.9 weeks), at which time 89% were breastfeeding, 21% were underweight, and 24% were stunted (Table 1). 1008 (76%) infants had mothers who had not yet initiated cART by infant enrollment (Figure 1).

Mothers were a median age of 31 years (IQR: 27-34 years) and had been enrolled in the UNC-DRC program for a median of 72 days (IQR: 0-126 days) at the time of infant enrollment (Table 1). The median enrollment duration was longer for mothers who initiated cART by infant enrollment than those who had not initiated cART (109 days versus 56 days). Baseline maternal CD4 count also differed, with a higher proportion of mothers who initiated cART having a CD4 cell count <350 cells/mm^3 than mothers who had not initiated cART (55% versus 30%). Mothers who initiated cART had been receiving cART for a median of 65 days (IQR: 32-102 days) by the time of infant enrollment.

Overall, 241 infants were LTFU over 13,365 person-months of follow-up and the unadjusted 18-month cumulative incidence of LTFU was 18% (95% CL: 16, 21%). Many infants (5% [95% CL: 4, 7%]) never returned for a visit after enrolling in care, 9% (95% CL: 8, 11%) were LTFU within three months, and 13% (95% CL: 11, 15%) were LTFU within six months. An assessment of the 18-month cumulative incidence of LTFU within strata of baseline covariates suggested that older infant enrollment age, younger maternal age, and shorter maternal duration in care were associated with increased LTFU (Table 2). There did not appear to be differences in the 18-month cumulative incidences of LTFU between strata of other covariates, including maternal CD4 cell count.

Figure 2 shows the 18-month cumulative incidence function for infant LTFU within strata of maternal cART status at the mean value of baseline covariates; the 18-month estimate was 8% (95% CL: 5, 11%) for infants whose mothers had initiated cART by baseline and 20% (95% CL: 17, 22%) for infants whose mothers had not yet initiated cART. In the unadjusted Fine and Gray subdistribution hazards model, the HR comparing LTFU among infants whose mothers did not receive cART by infant enrollment to those whose mothers did receive cART by infant enrollment was 2.42 (95% CL: 1.67, 3.64) (Table 3). Without imputing missing data, the covariate-adjusted HR was 3.13 (95% CL: 1.97, 4.98). After

multiple imputation was used to account for missing covariate data, the covariate-adjusted HR was 2.75 (95% CL: 1.81, 4.16). Using Cox regression, the unadjusted HR was 2.69 (95% CL: 1.78, 4.05), the covariate-adjusted HR excluding infants with missing covariate data was 3.22 (95% CL: 2.00, 5.18), and the covariate-adjusted HR using multiple imputation for missing data was 2.82 (95% CL: 1.83, 4.35).

In stratified analyses, we observed a protective effect of providing HIV-infected mothers with cART on LTFU of their HIV-exposed infants among both maternal CD4 groups (<350 and 350+) (Table 3). The association appeared stronger among infants whose mothers had a CD4 cell count ≥350 (subdistribution HR: 3.73 [95% CL: 1.76, 7.90]) at the time of infant enrollment compared to infants whose mothers had a CD4 cell count <350 (subdistribution HR: 2.14 [95%CI: 1.23, 3.70]).

DISCUSSION

In a large cohort of HIV-exposed infants in Kinshasa, DRC, we found that infants whose mothers had not yet initiated cART by infant enrollment were more than twice as likely to be LTFU than infants whose mothers had initiated cART. To our knowledge, this is the first study to report the cumulative incidence of infant LTFU within strata of maternal cART status and the first to quantify the association between maternal cART and LTFU of HIV-exposed infants.

Two prior studies suggested that maternal cART is predictive of successful EID. The first study, which included 217 mother-infant pairs from Mozambique, found that mothers who received cART were more likely to ever bring their infant for a virological test compared to women who did not receive cART, with an odds ratio (OR) of 3.15 (95% CL: 1.02-9.73). [22] A larger study that included 1,587 HIV-exposed infants in Cameroon examined the association between multiple predictors and having an incomplete EID process by seven months found that women who received no prophylaxis (OR: 2.3 [95% CL: 1.2-4.1]) or short-course prophylaxis (OR: 1.4 [95% CL: 0.9-2.1]) were more likely to have an incomplete EID process compared to women who received cART. [23]

While those prior studies provide evidence for an association between maternal cART and EID, HIV-exposed infant care involves more than a single testing event due to continued exposure to HIV through breastfeeding [24]. Regular follow-up of HIV-exposed infants is needed to administer additional HIV tests, communicate test results to caregivers, provide prophylactic drugs, and monitor breastfeeding. An important strength of our study is that we assessed LTFU through the entire HIV-exposed infant care cascade. Our findings suggest a strong beneficial effect of maternal cART on infant retention that persists beyond the initial HIV testing event. We observed that most infants who were LTFU were last seen at the clinic in the first six months of infant enrollment. Other studies have also described high rates of LTFU within the first few months. [2] To have the greatest impact on LTFU of HIV-exposed infants, HIV-infected mothers should be started on cART as early as possible.

Other strengths of our study are the large sample size, relatively long follow-up time, and use of competing risk methods. Whether or not providing HIV-infected mothers with cART

predicts LTFU of their HIV-exposed infants is a function of both the effect of maternal cART on infant LTFU and the effect of maternal cART on the competing events (e.g. death). [16] We chose to use the subdistribution hazards model described by Fine and Gray in our primary analysis over a traditional Cox regression model because doing so allowed us to interpret the hazard ratio as a measure of risk without the added assumption that the event of interest (LTFU) was independent of the competing events (death and graduation from care). Since competing risks are common in routine care settings, we consider the subdistribution HR more informative for policy decisions about PMTCT strategies than the cause-specific HR from a Cox model. However, as the distribution of competing events may vary between populations, we chose to additionally report cause-specific HRs. In our study, the subdistribution and cause-specific HRs were similar.

The study sites provided routine care to a patient population that was likely representative of other patient populations in Kinshasa. HIV services were integrated into the existing healthcare system and supervised by the government. However, there are two points to note about the generalizability of our findings. First, mother-infant pairs in this study received PMTCT services at centralized clinics providing family-centered care. The effect of maternal cART on infant LTFU may not be as strong in settings where infants and their mothers do not receive co-located care. Although our results are also not directly generalizable to programs providing decentralized care, we suspect that a similar reduction in infant LTFU could be achieved by providing newly enrolled mothers cART in that setting and future studies should assess this. Second, we excluded 116 infants who could not be matched to a mother also receiving care in the UNC-DRC program. It is likely that most of the excluded infants were orphans; however we could not confirm this in our study because the orphan status of infants was not routinely documented by the UNC-DRC program. Routine documentation of orphan status is needed so that future studies can assess how to provide optimal PMTCT care for HIV-exposed infants who may have lost one or more caregiver.

Our central hypothesis was that the propensity of mothers on cART to seek care was higher than that for mothers not yet on cART, and that this corresponded with an increased likelihood of continuing to bring their infants for care. The propensity of mothers on cART to seek care may differ between populations, for example due to factors such as cART eligibility criteria and how sick mothers are when they initiate treatment. Whether maternal cART is associated with reduced infant LTFU in other implementation contexts should be assessed. In the UNC-DRC program, cART was provided to mothers in accordance with national guidelines in effect at the time, which meant that mothers were eligible for cART based on established immunological or clinical criteria. We attempted to account for this by adjusting for maternal CD4 count in the analysis. We also examined stratified effect estimates and saw a strong protective effect of maternal cART on infant LTFU in both the low and high maternal CD4 groups, which suggests that cART eligibility criteria were not driving the observed associations. Moreover, maternal CD4 count at infant enrollment was not predictive of infant LTFU in our study population.

The UNC-DRC program made up to three attempts to track infants who missed clinic appointments in order to encourage retention in care and correctly classify the mortality

status of infants who died. Although we used statistical methods that accounted for known deaths (3% among infants whose mothers were on cART and 5% among infants whose mothers were not on cART), it should be noted that the mortality status of infants who were LTFU is by definition unknown. Indeed, LTFU includes both individuals who are alive and lost from care, as well as individuals who died but were misclassified as LTFU.[25] Thus it is not possible for us to tease out what portion of the effect of maternal cART on infant LTFU is attributable to differentials in mortality between the comparison groups versus other potential reasons for infant LTFU, such as those related to how cART affects the propensity of mothers to seek care for their children. These pathways should be assessed in future studies with dedicated resources for community-based tracing to determine the outcomes of HIV-exposed infants and their families.

Overall, our results suggest that providing cART to HIV-infected mothers may lead to improvements in the implementation of PMTCT care for HIV-exposed infants, including early infant diagnosis (EID) and timely cART initiation for those that are positive. This study specifically addressed the question of whether providing HIV-infected mothers with cART reduced LTFU of HIV-exposed infants after they presented to care. Another important loss point of HIV-exposed infants is the time between birth and uptake of follow-up care. Whether or not maternal cART could also improve linkages to follow-up care for HIV-exposed infants remains unknown and should be established in future studies.

Little is known about other factors that contribute to LTFU among HIV-exposed infants. There is evidence to suggest that addressing structural barriers including cost, transportation, waiting time, and service quality may improve retention in the PMTCT setting. [22,26-30] Addressing issues involving fatalistic attitudes around pediatric HIV and reducing fear of stigma and discrimination may also be important. [31]. Covariates in this study that appeared to predict infant LTFU were older infant enrollment age, younger maternal age, and maternal enrollment duration.

Despite the fact that LTFU of HIV-exposed infants is an ongoing public health problem, it remains inadequately studied in part because quality individual-level data from HIV-exposed infants are not widely available from field settings. The UNC-DRC program routinely collected prospective individual-level data on HIV-exposed infants and linked data between infants and their mothers. Such linkages are often difficult or impossible to obtain retrospectively, limiting the number of studies that are able to construct cohorts of mother-infant pairs in order to assess the impact that maternal factors have on infant outcomes. Routine quality improvement activities implemented at the UNC-DRC sites, including active tracking of patients who missed clinic appointments, also assured that the data included in the analyses were of high quality.

In conclusion, providing HIV-infected mothers with cART could increase retention in care of their HIV-exposed infants. This is an important collateral benefit that countries should consider as they make decisions around the provision of cART for all pregnant and breastfeeding women (Options B/B+). [32] As LTFU remains an important barrier to delivering optimal care for HIV-exposed infants, explicit interventions to improve retention

of HIV-exposed infants should be prioritized, particularly in settings where cART is not provided to all mothers.

Acknowledgments

FUNDING

L.F. was supported by a National Institutes of Health training grant (grant numbers 2T32AI070114-06, 5T32AI070114-07). The UNC-DRC program that provided data for this secondary analysis was funded by the Centers for Disease Control and Prevention President's Emergency Plan for AIDS Relief, with additional support from the Elizabeth Glaser Pediatric AIDS Foundation, the Belgian Development Cooperation, the William J. Clinton Foundation, the United Nations Children's Fund, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

ABBREVIATIONS

cART	combination antiretroviral therapy
CL	confidence limit
DRC	Democratic Republic of Congo
EID	early infant diagnosis
HR	hazard ratio
HAZ	height-for-age Z-score
IQR	interquartile range
LTFU	loss to follow-up
PMTCT	prevention of mother-to-child HIV transmission
UNC	University of North Carolina at Chapel Hill
WAZ	weight-for-age Z-score
WHO	World Health Organization

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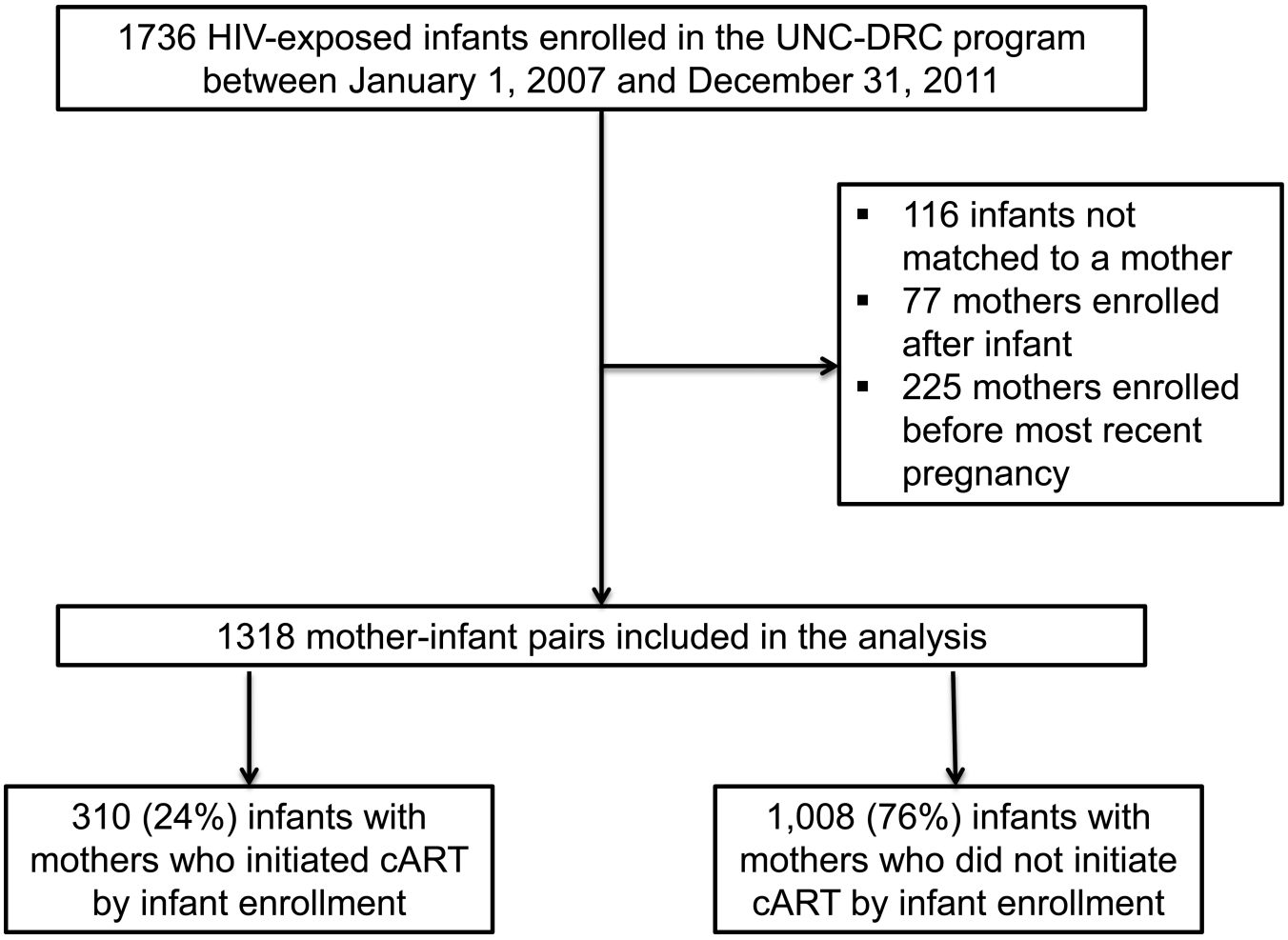
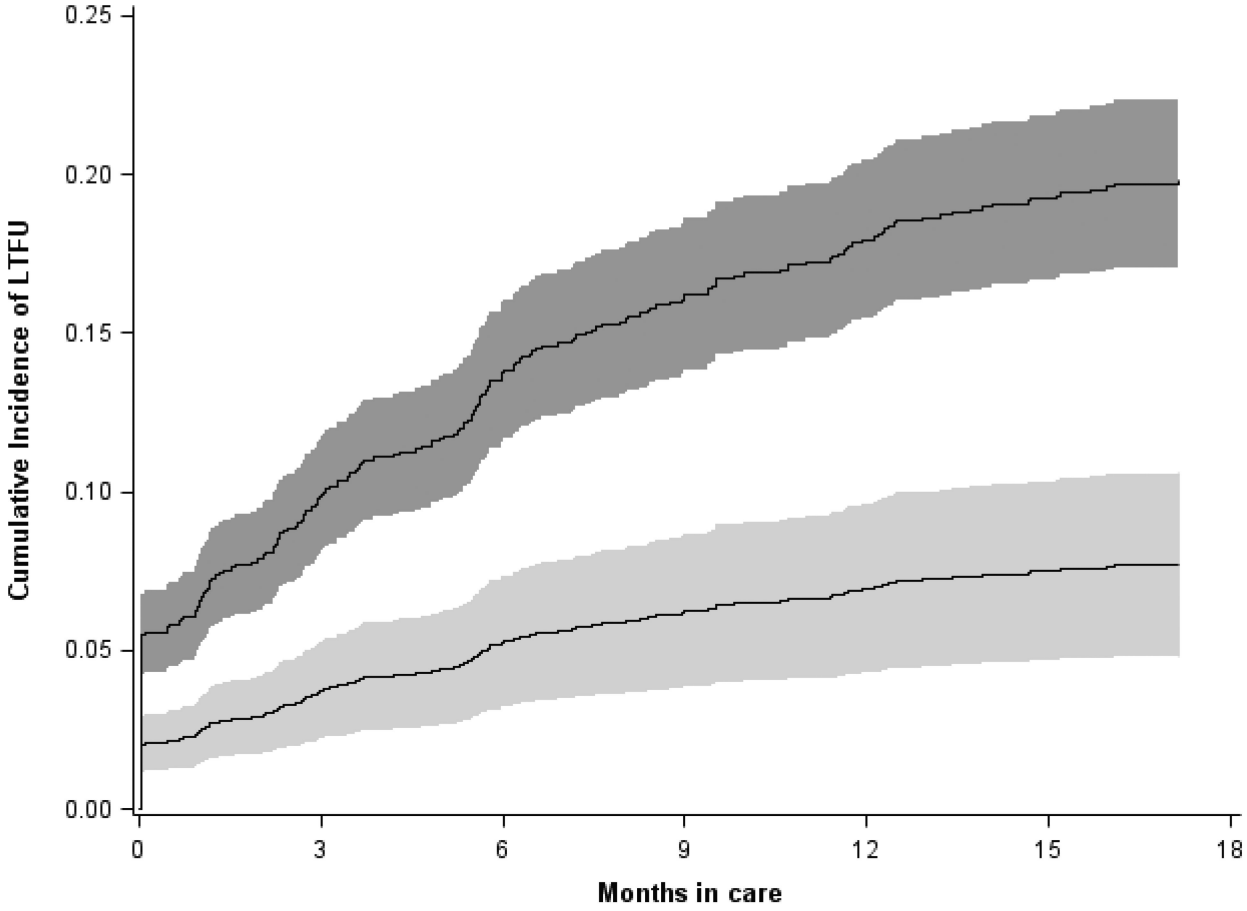


Abbreviations: UNC, University of North Carolina at Chapel Hill; DRC, Democratic Republic of Congo; cART, combination antiretroviral therapy.

Figure 1.
Flowchart depicting the study population.



a The cumulative incidence function is estimated at the mean values of baseline covariates, including infant age, infant weight-for-age Z score, maternal age, maternal CD4 count, maternal enrollment duration, and time since the beginning of the study.

Figure 2.

18-month cumulative incidence function of loss to follow-up among HIV-exposed infants in Kinshasa, Democratic Republic of Congo, plotted by maternal combination antiretroviral therapy (cART) status at infant enrollment into care [a].

Table 1

Characteristics of HIV-exposed infants and their mothers at infant enrollment into care, by maternal combination antiretroviral therapy status, Kinshasa, Democratic Republic of Congo.

	Maternal cART (N=310)	No Maternal cART (N=1008)	Overall (N=1318)
Median infant age in weeks (IQR)	2 (2, 3)	3 (2, 9)	3 (2, 7)
Calendar year at infant enrollment			
2007	15 (5)	112 (11)	127 (10)
2008	30 (10)	158 (16)	188 (14)
2009	65 (21)	279 (28)	344 (26)
2010	68 (22)	224 (22)	292 (22)
2011	132 (43)	235 (23)	367 (28)
Infant gender [N (%)]			
Female	156 (50)	513 (51)	669 (51)
Male	154 (50)	495 (49)	649 (49)
Any PMTCT regimen [N (%)]			
Yes	307 (99)	786 (86)	1093 (89)
No	3 (1)	127 (14)	130 (11)
Breastfeeding			
Yes	222 (91)	628 (89)	850 (89)
No	23 (9)	78 (11)	101 (11)
Infant underweight			
Yes	57 (19)	210 (22)	267 (21)
No	241 (81)	765 (78)	1006 (79)
Infant stunted			
Yes	66 (22)	236 (24)	302 (24)
No	231 (78)	737 (76)	968 (76)
Median maternal age in years [IQR]	32 (29-35)	30 (26-34)	31 (27-34)
Median days mother enrolled [IQR]	109 (74-141)	56 (0-115)	72 (0-126)
Median days mother on cART	65 (32-102)	N/A	N/A
Maternal CD4 count			
<350 cells/mm^3	163 (55)	278 (30)	441 (36)
350+ cells/mm^3	134 (45)	661 (70)	795 (64)

Abbreviations: cART, combination antiretroviral therapy; IQR, interquartile range; PMTCT, prevention of mother-to-child HIV transmission

Table 2

18-month cumulative incidence of loss to follow-up within strata of baseline covariates, Kinshasa, Democratic Republic of Congo.

	Cumulative incidence of LTFU	95% Confidence limit
Age at infant enrollment		
<4 weeks	17.1	(14.7, 19.8)
4+ weeks	20.9	(17.0, 24.6)
Calendar year at infant enrollment		
2007-2008	18.8	(14.7, 23.4)
2009-2011	18.4	(16.0, 20.9)
Underweight		
Yes	19.4	(14.8, 24.4)
No	18.2	(15.8, 20.6)
Age of mother at infant enrollment		
<30 years	21.3	(18.1, 24.7)
30+ years	16.2	(13.6, 19.0)
Enrollment duration of mother at infant enrollment		
<3 months	19.8	(17.1, 22.7)
3+ months	16.6	(13.6, 20.0)
Maternal CD4 count at infant enrollment		
<350 cells/mm^3	18.5	(14.7, 22.4)
350+ cells/mm^3	18.5	(15.7, 21.2)

Abbreviations: LTFU, loss to follow-up; PMTCT, prevention of mother-to-child transmission of HIV

Table 3

Estimated effect of maternal combination antiretroviral therapy on loss to follow-up of HIV-exposed infants in Kinshasa, Democratic Republic of Congo.

	LTFU (N)	Person-months of follow-up	Subdistribution hazard ratio	95% Confidence limit
Unadjusted Fine and Gray model				
No maternal cART	212	9539	2.42	(1.67, 3.64)
Maternal cART	29	3827	1.	
Covariate-adjusted Fine and Gray model, complete case[a]				
No maternal cART	178	8703	3.13	(1.97, 4.98)
Maternal cART	22	3575	1.	
Covariate-adjusted Fine and Gray model, multiple imputation[b]				
No maternal cART	212	9426	2.75	(1.81, 4.16)
Maternal cART	29	3795	1.	
Covariate-adjusted Fine and Gray model, multiple imputation, stratified by maternal CD4 at infant enrollment[c,d]				
CD4 <350, no maternal cART	65	2251	2.14	(1.23, 3.70)
CD4 <350, maternal cART	20	1927	1.	
CD4 350+, no maternal cART	147	7288	3.73	(1.76, 7.90)
CD4 350+, maternal cART	9	1899	1.	

Abbreviations: cART, combination antiretroviral therapy; LTFU, loss to follow-up

[a] Fine and Gray subdistribution proportional hazards model adjusted for baseline variables, including infant age, infant WAZ, maternal age, maternal CD4 count, maternal enrollment duration, and calendar time. Infants with missing covariate data (N=122) were excluded from the analysis.

[b] Fine and Gray subdistribution proportional hazards model adjusted for baseline variables, including infant age, infant WAZ, maternal age, maternal CD4 count, maternal enrollment duration, and calendar time. Missing data were imputed.

[c] Fine and Gray subdistribution proportional hazards model adjusted for baseline variables, including infant age, infant WAZ, maternal age, maternal enrollment duration, and calendar time. Missing data were imputed.

[d] Loss to follow-up counts and person-months of follow-up are the average from 5 imputed datasets.